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Case report

Disease progression or treatment-related complication? When mogamulizumab misleads in the management of Sézary syndrome: A case report

Dorota Woźniak[1,2], Mateusz Olek[1,2], Agnieszka Kędzior[1,2], Anastazja Szlauer-Stefańska[1]

[1]Department of Bone Marrow Transplantation and Oncohematology,
Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Poland
[2]RADIO(T)RACERS Students' Scientific Club, Department of Oncology,
Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland

Address for correspondence:
Dr n. med. Anastazja Szlauer-Stefańska
Klinika Transplantacji Szpiku i Onkohematologii
Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie
Państwowy Instytut Badawczy, Oddział w Gliwicach
ul. Wybrzeże Armii Krajowej 15, 44-102 Gliwice
tel. +48 32 278 85 60
e-mail: anastazja.szlauer@gliwice.nio.gov.pl

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ABSTRACT

Sézary syndrome (SS) is a cutaneous T-cell lymphoma characterized by aggressiveness, rarity, and poor outcome. When the disease becomes advanced (from stage IIB), mogamulizumab (MOGA) is a treatment option with potential adverse effects, including mogamulizumab-associated rash (MAR). The similarity between the symptoms of MAR and SS progression can lead to a delay in starting the next line of potentially effective treatment. This case illustrates the difficulties in distinguishing MAR from SS progression during MOGA treatment. In February 2024, a patient received an SS diagnosis, showing symptoms like erythroderma and inguinal lymphadenopathy. The flow cytometry confirmed the blood involvement. MOGA treatment began in April 2025, after three unsuccessful lines of systemic treatment. After the first cycle, the patient developed severe scaling, widespread erythroderma, and fever, raising concerns about MAR. MOGA was temporarily discontinued, and systemic corticosteroid therapy was initiated. A skin biopsy showed non-specific findings. One month later, MOGA was reintroduced, but new skin lesions appeared. Repeated histopathological examination pointed toward SS progression rather than a drug-related complication. The subsequent clinical course was complicated by bacteremia and secondary skin infections. Next, bridging therapy with bexarotene was initiated, and the patient was referred for allogeneic hematopoietic stem cell transplantation. This case emphasizes the diagnostic and treatment difficulties associated with overlapping clinical and histopathologic features of SS and MAR. It also underscores the importance of an individual approach, repeated clinicopathologic evaluations, and multidisciplinary collaboration. Thus, it may help improve treatment outcomes and patient prognosis.

KEYWORDS

mogamulizumab, mogamulizumab-associated rash, cutaneous T-cell lymphoma, adverse drug reaction, erythroderma, rash

INTRODUCTION

Sézary syndrome (SS) is a rare, aggressive form of cutaneous T-cell lymphoma with an as-yet unidentified etiology [1,2,3]. SS accounts for approximately 3% of all cutaneous lymphomas [3] and most commonly develops in adult men, typically in the fifth or sixth decade of life [2,3]. It is characterized by a triad of erythroderma, lymphadenopathy, and atypical T lymphocytes with “cerebriform” nuclei (Sézary cells) located in the lymph nodes, skin, and peripheral blood [1,2,3,4]. Apart from extensive skin lesions and pruritus, hepatosplenomegaly and general fatigue are also observed [3]. The diagnosis of SS requires fulfillment of specific hematologic criteria. Staging of SS

includes assessment of skin (T), lymph nodes (N), visceral organs (M), and blood (B) involvement [2,5].

In SS, first-line treatment combines systemic with skin-directed therapy. Recommendations include extracorporeal photopheresis (ECP), systemic agents (retinoids or interferon-α) with ECP or psoralen plus UVA, chlorambucil and prednisone, or low-dose methotrexate [6]. After failure of first-line therapy, targeted immunotherapy, such as mogamulizumab (MOGA), or chemotherapy may be used, and allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative option in selected cases [6]. MOGA, an alternative in second-line therapy [1,2,5,6], is a defucosylated, humanized IgG1 κ monoclonal antibody targeting the C-C chemokine receptor 4 (CCR4), with enhanced antibody-dependent cellular cytotoxicity. CCR4, involved in lymphocyte skin trafficking, is stably expressed on malignant T-cells in cutaneous lymphomas, including SS [6,7,8]. A common adverse effect of this therapy is mogamulizumab-associated rash (MAR), with varying clinical features that may resemble SS and thereby complicate treatment decisions [6,9].

Here, we report a case of SS treated with MOGA, highlighting the uncharacteristic clinical presentation and diagnostic challenges in the context of disease progression and suspected MAR.

CASE REPORT

A 51-year-old male with a two-year history of desquamation in the sternal region was admitted with erythroderma and inguinal lymphadenopathy. His history was significant for arterial hypertension, hypercholesterolemia, and nicotine addiction.

Flow cytometry revealed a distinct population of CD3+CD4+ cells without expression of CD7 and CD26, and an elevated CD4/CD8 ratio (5.5:1). In view of the clinical presentation and the presence of Sézary cells, in February 2024, the patient was diagnosed with SS stage IV (TNMB classification: T4N1M0B2). Initially, interferon-α was administered for 3 months without benefit. Gemcitabine in monotherapy was subsequently introduced. Due to disease progression, the patient received one cycle of cyclophosphamide, doxorubicin, vincristine, and prednisone.

Because of a lack of therapeutic response, additional testing was performed, including chest and abdominal computed tomography. As a result, the thrombus was detected in the internal jugular vein, for which low-molecular-weight heparin in a therapeutic dose was administered. Imaging also revealed a tuberculous cavity in the lung, consistent with a history of treated tuberculosis in 2024. Laboratory tests demonstrated persistent hepatitis B core antibody positivity and undetectable hepatitis B virus DNA level, prompting an initiation of lamivudine treatment. Considering these findings and a modified Severity Weighted Assessment Tool (mSWAT) score of 150, the patient was

deemed eligible for MOGA. Treatment was planned in 28-day cycles, with 1 mg/kg (total dose 60 mg) administered intravenously, beginning in April 2025 (Figure 1). Before the first infusion anti-pyretic (paracetamol 1000 mg) and antihistamine (clemastinum 2 mg) were administered. Subsequent infusions were not preceded by premedication. After four doses and completion of the first cycle, the patient experienced clinical deterioration, including febrile episodes and marked desquamation of previously regressed skin lesions. In view of clinical suspicion of MAR, a punch biopsy of the left lumbar skin was performed, and MOGA was discontinued; systemic dexamethasone therapy was started. The biopsy revealed non-specific findings, including acanthosis and the presence of T lymphocytes (CD4+, CD8+) in the epidermis. In the dermis, patchy infiltrates of small T lymphocytes were observed, with the immunophenotype CD3+, CD4+, variable expression of CD8, CD5+, CD7-, and PD1-.

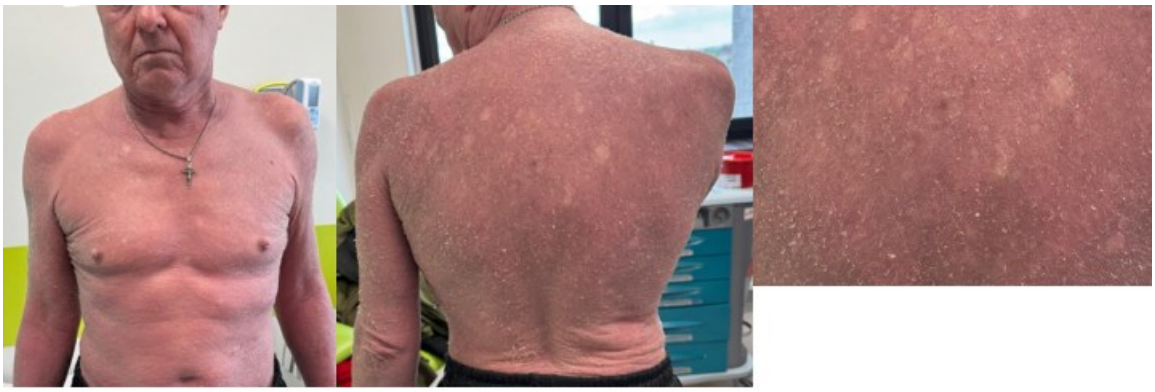

Fig. 1. The clinical presentation of the patient at the time of enrollment in mogamulizumab treatment in April 2025: erythroderma and infiltrative, desquamating lesions involving the entire skin surface, corresponding to a modified Severity Weighted Assessment Tool (mSWAT) score of 150. mSWAT reflects the extent of skin involvement in the treatment of primary cutaneous lymphomas. Also, numerous bilateral supraclavicular, inguinal, and axillary lymph nodes measuring up to 2 mm in diameter were palpated on physical examination.

Due to the lack of specific evidence supporting MAR, MOGA was reintroduced in June. However, further progression of skin lesions was observed, with intense skin flaking, facial edema, and irregular, violaceous patches located on the upper chest and back (Figure 2). Moreover, in the popliteal fossae, plaque-like infiltrates were present. A consulting dermatologist raised the possibility of a photoallergic reaction, although without exclusion of SS progression.

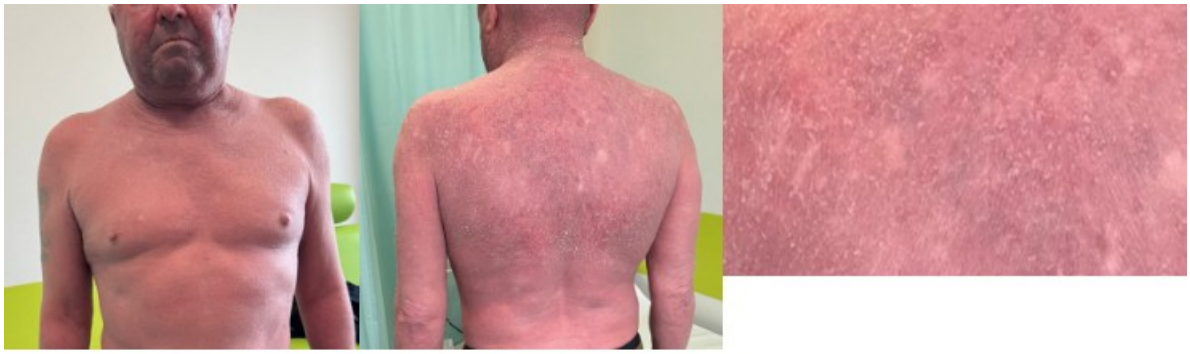

Fig. 2. The condition of the patient in June 2025 following reintroduction of mogamulizumab: presence of facial edema with unaffected palpebral fissures. Isolated dermal infiltrates that tend to coalesce but lack sharp demarcation and exudate. Patchy, violaceous infiltrates on the upper chest and back in a resolving phase corresponding to areas of normal skin. Desquamation is consistent with post-inflammatory changes. Mucous membranes are unremarkable. The overall clinical presentation may suggest a photoallergic reaction; however, without clarity and exclusion of progression of Sézary syndrome.

In the subsequent weeks, new nodular skin lesions were observed on the arm (Figure 3), thigh, and lower leg. Facial edema was accompanied by partial loss of eyebrows and eyelashes. Additional findings included desquamation, peripheral lymphadenopathy, onycholysis, nail dystrophy, and fissures on the hands and feet. The mSWAT score was 152 (0×1 + 74×2 + 1×4). Computed tomography with contrast showed lymph nodes of similar diameters as in baseline assessment, suggesting disease stagnation. Due to inconclusive results from the first biopsy, a repeat biopsy of a newly developed nodular lesion on the left arm was performed, revealing similar findings*:* medium and small-sized T-cells, including CD3+, CD4+, and CD8- in the superficial dermis with epidermotropism. Also, acanthosis and focal spongiosis with CD4+, CD8- T lymphocytes were observed in the epidermis. This time, the clinical and histopathologic findings were deemed consistent with the progression of SS rather than MAR.

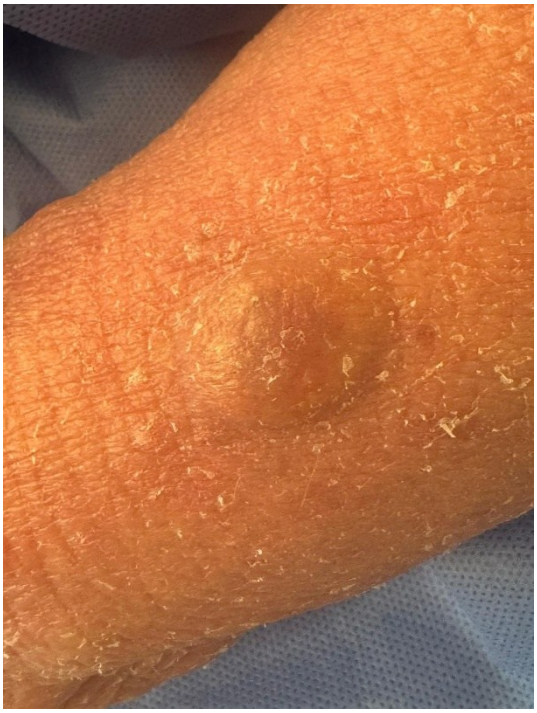

Fig. 3. Signs of Sézary syndrome progression at the end of mogamulizumab treatment in August 2025: newly developed prominent nodular cutaneous lesion on the left arm, up to 2 cm in diameter, accompanied by persistent erythroderma, desquamation and pruritus.

MOGA was discontinued, with the last dose administered in July. Subsequently, the patient was hospitalized for bacteremia and skin infection with impaired renal function. Bexarotene was introduced as the next-line treatment. The patient's sister was identified as a fully-matched donor, and he was planned to undergo allo-HSCT; however, no follow-up data were available at the time of manuscript preparation.

DISCUSSION

Primary cutaneous lymphomas, including T-cell lymphomas, represent a heterogeneous group of diseases that differ in their clinical manifestations and prognosis. The course of these disorders is typically chronic, and a complete cure is rarely achieved [2,7]. Furthermore, the rarity, heterogeneity, stage of disease, and clinical presentation of primary cutaneous lymphomas, such as SS, pose diagnostic and therapeutic challenges, often requiring an interdisciplinary approach to patient management [2,6]. An additional difficulty in SS is the high frequency of disease relapse and poor overall survival, with a median of less than five years in advanced stages [2,3,7].

The symptoms of SS significantly impair patients' quality of life. Although treatment may be effective, it is primarily palliative in nature [6,9]. The selection of an appropriate therapeutic strategy, considering the clinical presentation and disease stage, may be challenging, particularly for second-line therapy after failure of systemic treatment [6,7].

One of the targeted immunotherapy options in the second-line treatment of SS is MOGA, a monoclonal antibody against CCR4 expressed on lymphoma cells, that enhances antibody-dependent cellular cytotoxicity directed against those cells [6,10,11]. Despite its fundamental role, clinical response to MOGA does not appear to be related in CCR4 expression in the skin. The safety and efficacy of MOGA have been demonstrated in the MAVORIC study, which showed the superiority of the drug, with a median duration of response of 3 months and overall response rate of 28% [6,7,9,11]. The approval of this drug extends to Europe for the treatment of adults with mycosis fungoides (MF) or SS with at least one failed prior systemic therapy [6]. It should be noted that, despite its overall good tolerability, MOGA is associated with certain adverse events leading to discontinuation in 19% of patients. According to the MAVORIC trial, the most common of these are infusion-related reactions, rash, diarrhea, and fatigue [7,9]. Additionally, attention should be paid to the interval between MOGA therapy and allo-HSCT due to the risk of acute graft-versus-host disease [9,11,12].

One of the most common adverse effects of MOGA is MAR, which is presumed to reduce regulatory T-cells in the skin, allowing cytotoxic T-cells to cause inflammation and skin disease [6,9]. MAR occurs a few weeks after initiation of MOGA treatment in approximately 8% of patients and is characterized by superficial dermal infiltration with enlarged lymphocytes and histiocytes [9,13,14]. It is typically managed with topical or systemic corticosteroids and, in moderate and severe forms, interruption of MOGA [9]. However, MAR may be easily mistaken for other diseases due to a lack of characteristic clinical presentation. Psoriasis vulgaris, pustular psoriasis, impetiginization, or the erythrodermic form of MF should be considered during the diagnostic process. Also, in clinical assessment of the rash and its worsening, the potential contribution of other drugs and interactions should be considered. In this context, lamivudine may represent a possible contributing factor. However, the treatment had been initiated before the start of MOGA therapy, without any evident adverse effects being observed. It is indicated that lamivudine has rarely been associated with cutaneous adverse reactions such as skin rash, with most reported cases occurring in HIV-infected patients [15]. Moreover, MAR can mimic the progression of SS, appearing as erythematous macules or scaly lesions, or as a rare photo-distributed pruritic rash, often with visible hair loss [9,10,16]. Due to the possible development of life-threatening and rarely reported complications, such as toxic epidermal necrolysis or Stevens-Johnson syndrome, differentiating MAR from the progression of SS seems to be essential [9]. Skin biopsy is a key diagnostic tool in differentiating MAR from disease progression [13]. In histopathological examination, MAR presents as spongiotic or psoriasiform dermatitis, lichenoid CD8+ interface dermatitis, or granulomatous infiltrates composed of epithelioid histiocytes. In SS, CD4+ cells are

dominant, with loss of CD7 expression, whereas in MAR, CD8+ cells are more characteristic, with preserved expression of CD7. In a case of an inconclusive biopsy result, a repeat biopsy should be considered during treatment for SS and/or MAR [9].

In this case, the rash in question was characterized by erythematous scaly lesions, which could represent either MAR or progression of SS. While awaiting the results of the first biopsy, MOGA was temporarily discontinued, as advised for grade 3 rash [9]. After the inconclusive biopsy and the lack of definitive clinical features, MOGA was reintroduced. Further progression of clinical presentation with involvement of larger areas of skin and hair loss prompted the second biopsy, which suggested progression of SS rather than MAR.

CONCLUSIONS

This case shows that MAR requires vigilance, but excessive caution and early discontinuation of MOGA also carry risks.

Our case highlights the difficulties and importance of an individualized approach, the limitations of current diagnostic tools, and the need for clinical experience in differentiating MAR from SS progression.

Collaboration between oncology, dermatology, and pathology physicians should underpin clinical decision-making. It may improve the quality of life and potentially prolong survival in patients with SS.

Informed consent statement

The patient provided written informed consent for publication of images and other clinical information.

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Conflict of interest

The authors declare no conflict of interest regarding this manuscript.

Authors' contribution

Study design – D. Woźniak, A. Szlauer-Stefańska
Manuscript preparation – D. Woźniak, M. Olek, A. Kędzior, A. Szlauer-Stefańska
Literature research – D. Woźniak, M. Olek

Final approval of the version to be published – D. Woźniak, M. Olek, A. Kędzior, A. Szlauer-Stefańska

REFERENCES

1. NCCN Guidelines for Patients® Cutaneous T-Cell Lymphomas. Fort Washington, PA: National Comprehensive Cancer Network, 2024.

2. Sokołowska Wojdyło M, Olszewska B, Chmielowska E, Robak E, Prochorec-Sobieszek M, Kamińska-Winciorek G, et al. Primary cutaneous lymphomas. Diagnostic and therapeutic guidelines of the Polish Dermatological Society (PTD) and Polish Lymphoma Research Group (PLRG). Dermatol Rev./Przegl Dermatol. 2023;110(6):647–674. doi: 10.5114/dr.2023.138937.

3. Sézary syndrome – Orphanet. Orphanet Encyclopaedia; 3162 [online] https://www.orpha.net/en/disease/detail/3162?name=sezary&mode=name (accessed Jan 2026).

4. Campbell JJ, Clark RA, Watanabe R, Kupper TS. Sézary syndrome and mycosis fungoides arise from distinct T-cell subsets: a biologic rationale for their distinct clinical behaviors. Blood. 2010;116(5):767–771. doi: 10.1182/blood-2009-11-251926.

5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Primary Cutaneous Lymphomas, Version 1.2025. Fort Washington, PA: National Comprehensive Cancer Network, 2025.

6. Latzka J, Assaf C, Bagot M, Cozzio A, Dummer R, Guenova E, et al. EORTC consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome – update 2023. Eur J Cancer. 2023;195:113343. doi: 10.1016/j.ejca.2023.113343.

7. Kim YH, Bagot M, Pinter-Brown L, Rook AH, Porcu P, Horwitz SM, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. Lancet Oncol. 2018;19(9):1192–1204. doi: 10.1016/S1470-2045(18)30379-6.

8. Duvic M, Evans M, Wang C. Mogamulizumab for the treatment of cutaneous T-cell lymphoma: recent advances and clinical potential. Ther Adv Hematol. 2016;7(3):171–174. doi: 10.1177/2040620716636541.

9. Musiek ACM, Rieger KE, Bagot M, Choi JN, Fisher DC, Guitart J, et al. Dermatologic events associated with the anti-CCR4 antibody mogamulizumab: characterization and management. Dermatol Ther (Heidelb). 2022;12(1):29–40. doi: 10.1007/s13555-021-00624-7.

10. Hirotsu KE, Neal TM, Khodadoust MS, Wang JY, Rieger KE, Strelo J, et al. Clinical Characterization of Mogamulizumab-Associated Rash During Treatment of Mycosis Fungoides or Sézary Syndrome. JAMA Dermatol. 2021;157(6):700–707. doi: 10.1001/jamadermatol.2021.0877.

11. Larocca C, Kupper TS, LeBoeuf NR. Mogamulizumab Forecast: Clearer Patients, with a Slight Chance of Immune Mayhem. Clin Cancer Res. 2019;25(24):7272–7274. doi: 10.1158/1078-0432.CCR-19-2742.

12. Dai J, Almazan TH, Hong EK, Khodadoust MS, Arai S, Weng WK, et al. Potential association of anti-CCR4 antibody mogamulizumab and graft-vs-host disease in patients with mycosis fungoides and Sézary syndrome. JAMA Dermatol. 2018;154(6):728–730. doi: 10.1001/jamadermatol.2018.0884.

13. Beylot-Barry M, Quereux G, Nardin C, Duval-Modeste AB, Dereure O, Dalac-Rat S, et al. Effectiveness of mogamulizumab in patients with Mycosis Fungoides or Sézary syndrome: A multicentre, retrospective, real-world French study. J Eur Acad Dermatol Venereol. 2023;37(9):1777–1784. doi: 10.1111/jdv.19134.

14. Pilkington J, Ly S, Kayishunge D, Gentille C, Wong HK. Mogamulizumab in combination improves clinical outcomes in relapsed and refractory Sézary syndrome. Front Hematol. 2025;4:1557641. doi: 10.3389/frhem.2025.1557641.

15. Modak D, Guha SK. Severe skin rash with lamivudine in HIV infected patients: some unusual case reports. Indian J Pharmacol. 2013;45(3):298–300. doi: 10.4103/0253-7613.111906.

16. Mitteldorf C. Novel and recurrent histopathologic patterns of mogamulizumab-associated rash: diagnostic implications and insights for accurate diagnosis. J Dtsch Dermatol Ges. 2025;23(8):942–956. doi: 10.1111/ddg.15773.